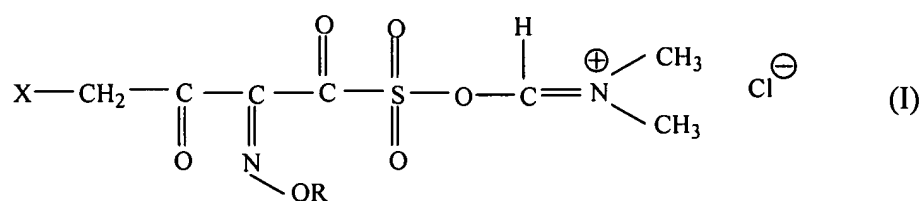


### **Amendments to the Claims:**

This listing of claims will replace all prior versions and listings of claims in the application.

**Listing of Claims:**

1. (Original) A novel 4-halo-2-oxyimino-3-oxo butyric acid-N, N-dimethyl formiminium chloride chlorosulfate of formula (I) useful in the preparation of cephalosporin antibiotics



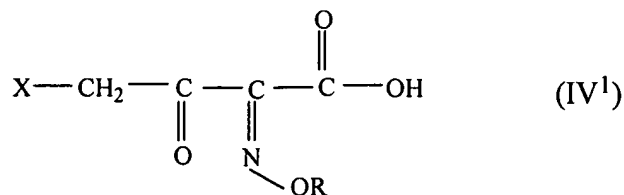
wherein

X is chlorine or bromine;

R is hydrogen, C<sub>1-4</sub> alkyl group, an easily removable hydroxyl protective group, -CH<sub>2</sub>COOR<sub>5</sub>, or -C(CH<sub>3</sub>)<sub>2</sub>COOR<sub>5</sub>

wherein R<sub>5</sub> is hydrogen or an easily hydrolysable ester group.

2. (Original) A process for preparation of compound of formula (I) comprising reacting 4-halo-2-oxyimino-3-oxobutyric acid of formula (IV<sup>1</sup>),



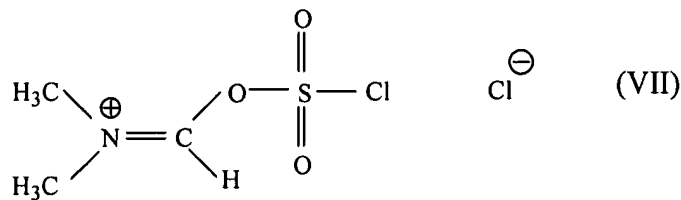
wherein

X is chlorine or bromine;

R is hydrogen, C<sub>1-4</sub> alkyl group, an easily removable hydroxyl protective group, -CH<sub>2</sub>COOR<sub>5</sub>, or -C(CH<sub>3</sub>)<sub>2</sub>COOR<sub>5</sub>

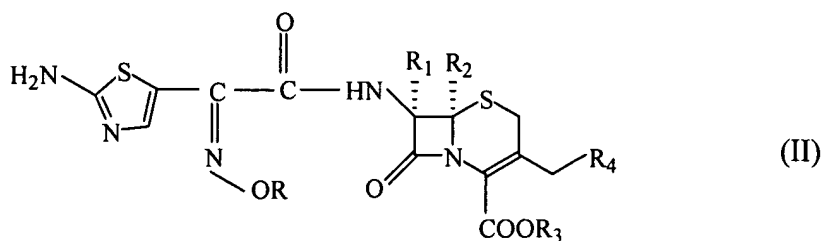
wherein R<sub>5</sub> is hydrogen or an easily hydrolysable ester group.

with N, N-dimethylformiminium chloride chlorosulphate of formula (VII)



in an organic solvent at a temperature ranging from  $-30^{\circ}\text{C}$  to  $-15^{\circ}\text{C}$ .

3. (Original) A process according to Claim 2, wherein the organic solvent is selected from chlorinated solvents such as dichloromethane, dichloroethane, or chloroform; aromatic hydrocarbons such as benzene or toluene; and nitriles such as acetonitrile, propionitrile or butyronitrile.
4. (Original) A process according to Claim 2, wherein the molar ratio of compound of formula (VII) to compound of formula (IV<sup>1</sup>) is between 1.1 to 1.3.
5. (Original) A process for preparation of a cephalosporin compound of formula (II),



wherein

R is hydrogen, C<sub>1-4</sub> alkyl group, an easily removable hydroxyl protective group, -CH<sub>2</sub>COOR<sub>5</sub>, or -C(CH<sub>3</sub>)<sub>2</sub>COOR<sub>5</sub>

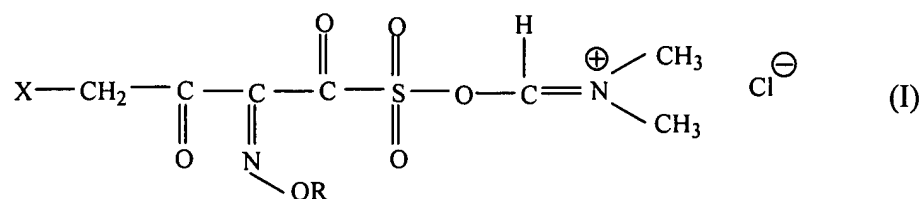
wherein R<sub>5</sub> is hydrogen or an easily hydrolysable ester group.

R<sub>1</sub> is hydrogen or -OCH<sub>3</sub>;

R<sub>2</sub> is hydrogen;

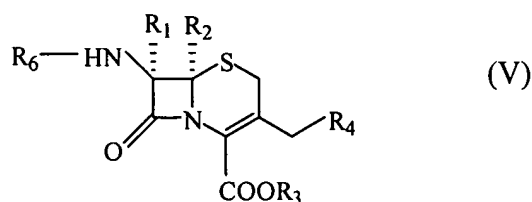
R<sub>3</sub> is hydrogen, a negative charge or together with the COO<sup>-</sup> group to which R<sub>3</sub> is attached is an ester, or an alkali or alkaline earth metal,

R<sub>4</sub> is hydrogen or is a substituent useful in cephalosporin chemistry;  
comprising reaction of compound of formula (I)



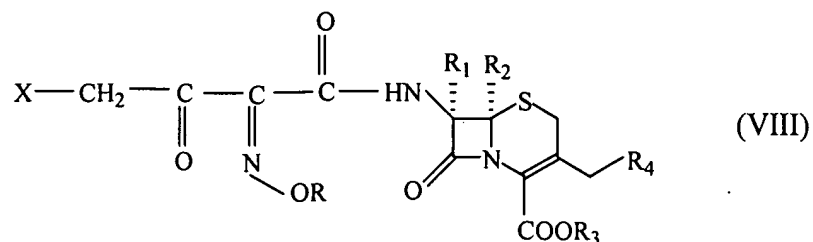
wherein X is chlorine or bromine; R is hydrogen, C<sub>1-4</sub> alkyl group, an easily removable hydroxyl protective group, -CH<sub>2</sub>COOR<sub>5</sub>, or -C(CH<sub>3</sub>)<sub>2</sub>COOR<sub>5</sub>, wherein R<sub>5</sub> is hydrogen or an easily hydrolysable ester group

with 7-amino cephalosporanic acid of formula (V),



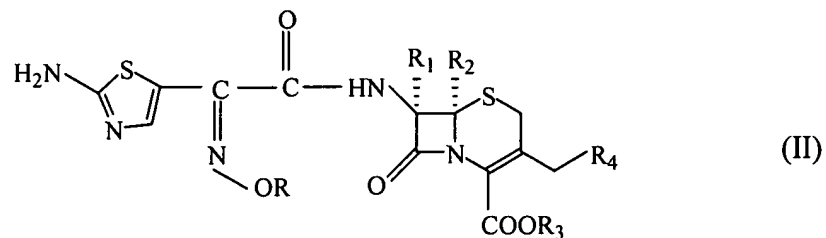
wherein R<sub>1</sub> is hydrogen or -OCH<sub>3</sub>; R<sub>2</sub> is hydrogen; R<sub>3</sub> is hydrogen, a negative charge or together with the COO<sup>-</sup> group to which R<sub>3</sub> is attached is an ester, or an alkali or alkaline earth metal, or is a silyl group; R<sub>4</sub> is hydrogen or is a substituent useful in cephalosporin chemistry; R<sub>6</sub> is hydrogen or a silyl group with the proviso that, when R<sub>3</sub> is hydrogen R<sub>6</sub> is also hydrogen; when R<sub>3</sub> is a silyl group R<sub>6</sub> is also a silyl group; and when R<sub>3</sub> is an ester, or an alkali or alkaline earth metal R<sub>6</sub> is hydrogen

to give 7-[(4-halo-2-oxyimino-3-oxobutyramido-3-substituted-3-cephem-4-carboxylic acid of formula (VIII),



wherein X, R, R<sub>1</sub>, R<sub>2</sub> and R<sub>4</sub> have the same meanings as defined hereinafter, and R<sub>3</sub> is hydrogen, a negative charge or together with the COO<sup>-</sup> group to which R<sub>3</sub> is attached is an ester, or an alkali or alkaline earth metal.

followed by cyclisation of compound (VIII) with thiourea to give compound of formula (II),



wherein R and R<sub>5</sub> are as defined above; R<sub>1</sub> is hydrogen or -OCH<sub>3</sub>; R<sub>2</sub> is hydrogen; R<sub>3</sub> is hydrogen, a negative charge or together with the COO<sup>-</sup> group to which R<sub>3</sub> is attached is an ester or an alkali or alkaline earth metal; R<sub>4</sub> is hydrogen or is a substituent useful in cephalosporin chemistry.

6. (Original) A process according to Claim 5, wherein the reaction of compound (I) and compound (V) to give compound (VIII) is carried out in an organic solvent and in the presence of a base at a temperature ranging from -80<sup>0</sup> C to -15<sup>0</sup> C,.
7. (Currently Amended) A process according to Claims 5 or 6, wherein the organic solvent is selected from chlorinated solvents such as dichloromethane, dichloroethane, and chloroform; aromatic hydrocarbons such as benzene and toluene; nitrile solvents such as acetonitrile, propionitrile and butyronitrile; ethers such as tetrahydrofuran and dioxane.

8. (Currently Amended) A process according to Claims 5 ~~or~~ 6, wherein the base is selected from N, N dimethyl aniline, diethyl amine, and pyridine.
9. (Currently Amended) A process according to Claims 5 ~~or~~ 6, wherein the molar ratio of compound (I) to the cephalosporin compound (V) is between 1.1 to 2.0, preferably between 1.2 to 1.5.
10. (Currently Amended) A process according to Claims 5 ~~or~~ 6, wherein the preferred temperature is between  $-55^{\circ}\text{C}$  to  $-25^{\circ}\text{C}$ .
11. (Original) A process according to Claim 5, wherein the reaction of compound (VIII) and thiourea to give the cephalosporin compounds of formula (II) is carried out in a mixture of organic solvent and water and in the presence of a base at low to ambient temperature.
12. (Currently Amended) A process according to Claims 5 ~~or~~ 11, wherein the the organic solvent is selected from chlorinated solvents such as dichloromethane, dichloroethane, and chloroform; aromatic hydrocarbons such as benzene and toluene; nitrile solvents such as acetonitrile, propionitrile and butyronitrile; ethers such as tetrahydrofuran and dioxane.
13. (Currently Amended) A process to Claims 5 ~~or~~ 11, wherein the base is selected from alkali metal carbonates, such as sodium carbonate, potassium carbonate and lithium carbonate; alkali metal hydrogen carbonates, such as sodium hydrogen carbonate and potassium carbonate; and alkali metal acetates, such as sodium acetate and potassium acetate.
14. (Currently Amended) A process according to Claims 5 ~~or~~ 11, wherein the temperature is between  $-5^{\circ}\text{C}$  to  $40^{\circ}\text{C}$ , preferably between  $-10^{\circ}\text{C}$  to  $30^{\circ}\text{C}$ .
15. (Original) A process according to Claim 5, wherein the compound of formula (II) is any one of
  - i) 7-[(Z)-2-(2-aminothiazol-4-yl)-2-hydroxyiminoacetamido]-3-vinyl-3-cephem-4-carboxylic acid i.e. cefdinir,

- ii) 7-[(Z)-2-(2-amino-4-thiazolyl)-2-methoxyimino]acetyl]amino-3-[(1Z)-2-(4-methyl-5-thiazolyl)ethenyl]-3-cephem-4-carboxylic acid, i.e. cefditoren and the pivaloyloxymethyl ester i. e. cefditoren pivoxil,
- iii) 7-[(Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetamido]-3-(1-methylpyrrolodino) methyl-3-cephem-4-carboxylate i.e. cefepime,
- iv) 7-[(Z)-2-(2-aminothiazol-4-yl)methoxyiminoacetamido]-3-methyl-3-cephem-4-carboxylic acid i.e. cefetamet, and the pivaloyloxymethyl ester i. e. cefetamet pivoxil,
- v) 7-[(Z)-2-(2-aminothiazol-4-yl)-2-carboxymethoxyiminoacetamido]-3-vinyl-3-cephem-4-carboxylic acid i.e. cefixime,
- vi) 7-[(Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetamido]-3-[[1-methyl-1H-tetrazol-5-yl]thio]methyl]-3-cephem-4-carboxylic acid i.e. cefmenoxime,
- vii) 7-[(Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetamido]-3-[[[5-carboxymethyl]-4-methyl-2-thiazolyl]thio]methyl]-3-cephem-4-carboxylic acid i.e. cefodizime,
- viii) 7-[(Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetamido]-3-[[2,3-dihydro-2-(2-hydroxyethyl)-3-imino-1H-pyrazol-1-yl]methyl]-3-cephem-4-carboxylic acid i. e. cefoselis,
- ix) 7-[(Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetamido]cephalosporanic acid i.e. cefotaxime,
- x) 7-[(Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetamido]-3-[9,2,3-cyclopenteno-1-pyridinium)methyl]-3-cephem-4-carboxylic acid i.e. cefpirome,

- xi) 7-[(Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetamido]-3-methoxymethyl-3-cephem-4-carboxylate- i.e. cefpodoxime and the 1-methylethoxycarbonyloxy ether i. e. cefpodoxime proxetil,
- xii) 7-[(Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetamido]-3-[[1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl-5,6,7-tetrahydroquinolinium-4-carboxylic acid inner salt i. e. cefquinome,
- xiii) 7-[(Z)-2-(2-aminothiazol-4-yl)-2-(1-carboxy-1-methylethyl)oximinoacetamido]-3-[pyridinium]methyl-3-cephem-4-carboxylic acid inner salt i. e. ceftazidime,
- xiv) 7-[(Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetamido]-3-[2-(5-methyl-1,2,3,4-tetrazoyl)-methyl-3-cephem-4-carboxylic acid i. e. ceftaram and the and the pivaloyloxymethyl ester i. e. ceftaram pivoxil,
- xv) 7-[(Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetamido]-3-[[2-furanylcarbonyl)thio]methyl]- 3-cephem-4-carboxylic acid i. e. ceftiofur,
- xvi) 7-[(Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetamido]-3-cephem-4-carboxylic acid i. e. ceftizoxime,
- xvii) 7-[(Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetamido]-3-[[2,5-dihydro-6-hydroxy-2-methyl-5-oxo-as-triazin-3-yl)thio]methyl]-3-cephem-4-carboxylic acid i. e. ceftriaxone, and
- xviii) 7-[(Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetamido]-3-[(1,2,3-thiadiazol-5-ylthio)methyl]- 3-cephem-4-carboxylic acid i. e. cefuzonam.